

09/825989

L16 ANSWER 7 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
 DUPLICATE 3
 ACCESSION NUMBER: 97:882691 SCISEARCH
 THE GENUINE ARTICLE: YH162
 TITLE: Enzymatic, chemical, and thermal breakdown of
 H-3-labeled glucobrassicin, the parent indole
glucosinolate
 AUTHOR: Chevolleau S (Reprint); Gasc N; Rollin P; Tulliez J
 CORPORATE SOURCE: INRA, LAB XENOBIOT, BP 3, F-31931 TOULOUSE 9, FRANCE
 (Reprint); UNIV ORLEANS, ICOA, UPRESA 6005, F-45067
 ORLEANS 2, FRANCE
 COUNTRY OF AUTHOR: FRANCE
 SOURCE: JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (NOV
 1997) Vol. 45, No. 11, pp. 4290-4296.
 Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW,
 WASHINGTON, DC 20036.
 ISSN: 0021-8561.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: LIFE; AGRI
 LANGUAGE: English
 REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The enzymatic, chemical, and thermal breakdown pathways of
 glucobrassicin, the major indolylmethyl **glucosinolate** of
 cruciferous vegetables, have been studied using synthetic
 H-3-labeled glucobrassicin (GBS). Radio-HPLC was used to analyze
 qualitatively and quantitatively the resulting products as well as
 their kinetics of formation. Enzymatic breakdown of GBS under
myrosinase action gave rise to different indole compounds
 [indole-3-carbinol (I3C), indole-3-**acetonitrile** (IAN) and
 3,3'-diindolylmethane (DIM)]. At neutral pH, GBS degradation was
 almost complete after 1 h, and the major breakdown product was I3C,
 which could be converted to DIM. The formation of this
 self-condensation product was observed as photosensitive. In acidic
 conditions, enzymatic degradation of GBS was a slower phenomenon,
 requiring 24 h to be nearly complete. IAN and I3C were the only two
 products occurring, and it was observed that the light had no effect
 either on the rate of formation or on the relative proportions of
 the breakdown products observed. GBS appeared as a very stable
 compound since no chemical degradation could be observed after 2 h
 in different aqueous media with pH in the 2-11 range. Moreover,
 after exposure to heat treatment, GBS was weakly degraded (10% in 1
 h), giving risk to a new minor indole condensation product
 corresponding to a 3-(indolylmethyl)glucobrassicin (IM-GBS).

L16 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on
 STN DUPLICATE 4
 ACCESSION NUMBER: 1997:41907 BIOSIS
 DOCUMENT NUMBER: PREV199799333895
 TITLE: Simultaneous determination of **isothiocyanates**
 , indoles, and oxazolidinethiones in
myrosinase digests of rapeseeds and rapeseed
 meal by HPLC.
 AUTHOR(S): Matthaeus, B. [Reprint author]; Fiebig, H.-J.
 CORPORATE SOURCE: Institut fuer Chemie und Physik der Fette,

Searcher : Shears 571-272-2528

09/825989

Bundesanstalt fuer Getreide- Kartoffel- und
Fettforschung, Postfach 1705, D-48006 Muenster,
Germany

SOURCE: Journal of Agricultural and Food Chemistry, (1996)
Vol. 44, No. 12, pp. 3894-3899.
CODEN: JAFCAU. ISSN: 0021-8561.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 25 Mar 1997

AB HPLC has been used for the analysis of **isothiocyanates**,
indoles, and oxazolidinethiones in rapeseeds and rapeseed meal. The
samples were treated with **myrosinase** and the released
hydrolysis products extracted with dichloromethane. The separation
was performed on an RP-18 column using a gradient system with
acetonitrile and water. Use of a programmable UV detector
permitted the detection of the compounds at their absorption maxima
of 210 and 240 nm, respectively. Response factors of eight standard
compounds were calculated for 240 nm. The contents of
glucosinolates calculated with the results of this method
showed a significant linear correlation ($r = 0.9995$; $P \leq 0.005$)
with the contents of **glucosinolates** evaluated with the
results of the HPLC method of desulfoglucosinolates.

L16 ANSWER 9 OF 16 CABA COPYRIGHT 2004 CABI on STN

ACCESSION NUMBER: 92:146229 CABA

DOCUMENT NUMBER: 19921452451

TITLE: Formation of indole **glucosinolates**
breakdown products during processing treatment
in cruciferous vegetables

AUTHOR: Shim, K. H.; Kang, K. S.; Sung, N. K.; Seo, K.
I.; Moon, J. S.

CORPORATE SOURCE: Department of Food Science and Technology,
Gyeongsang National University, Jinju 660-701,
Korea Republic.

SOURCE: Journal of the Korean Society of Food and
Nutrition, (1992) Vol. 21, No. 1, pp. 49-53.
14 ref.
ISSN: 0253-3154

DOCUMENT TYPE: Journal

LANGUAGE: Korean

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19941101
Last Updated on STN: 19941101

AB The released amount of thiocyanate ion in cruciferous vegetables
treated by wet heat, increased as a function of time and reached a
maximum value after 30 min, but did not change after dry heat
treatment. When samples were autolysed by **myrosinase**, the
amount of thiocyanate ion increased gradually, reached a maximum
value after 3 h and was higher than those treated by wet heat. The
released amount of thiocyanate ion in each sample was greatest in
cabbage, Chinese cabbage, radish, kale and mustard in that order.
The generated amount of indoleacetonitrile by heat treatment
increased as time elapsed, and the generated amount in each sample
was highest in cabbage, Chinese cabbage and radish, in that order.

Searcher : Shears 571-272-2528

09/825989

L16 ANSWER 10 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
 ACCESSION NUMBER: 91:302382 SCISEARCH
 THE GENUINE ARTICLE: FM516
 TITLE: ROLE OF **GLUCOSINOLATES** IN THE FORMATION OF
 N-NITROSO COMPOUNDS
 AUTHOR: TIEDINK H G M (Reprint); MALINGRE C E; VANBROEKHOVEN
 L W; JONGEN W M F; LEWIS J; FENWICK G R
 CORPORATE SOURCE: AGR UNIV WAGENINGEN, DEPT TOXICOL, POB 8129, 6700 EV
 WAGENINGEN, NETHERLANDS (Reprint); CTR AGROBIOL RES,
 6700 AA WAGENINGEN, NETHERLANDS; AGROTECH RES INST,
 6700 AA WAGENINGEN, NETHERLANDS; AFRC, INST FOOD
 RES, NORWICH NR4 7UA, NORFOLK, ENGLAND
 COUNTRY OF AUTHOR: NETHERLANDS; ENGLAND
 SOURCE: JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (1991)
 Vol. 39, No. 5, pp. 922-926.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: LIFE; AGRI
 LANGUAGE: ENGLISH
 REFERENCE COUNT: 28

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The hydrolysis of the **glucosinolates**, sinigrin,
 gluconapin, glucobrassicinapin, progoitrin, glucotropaeolin,
 sinalbin, gluconasturtiin, glucobrassicin, and 4-
 hydroxyglucobrassicin, by **myrosinase** from white mustard
 (*Sinapis alba*) or acid was examined. While all
glucosinolates were hydrolyzed by **myrosinase**, only
 4-hydroxyglucobrassicin, glucosinalbin, gluconasturtiin,
 glucobrassicin, and progoitrin were partially hydrolyzed by acid (pH
 2). When intact **glucosinolates** or **myrosinase**
 -treated **glucosinolate** products were treated with nitrite,
 only glucobrassicin and 4-hydroxyglucobrassicin formed N-nitroso
 compounds. The nitrosated products of **myrosinase**-treated
 glucobrassicin alone were mutagenic and induced about 400 *Salmonella*
typhimurium TA100 revertants/ μ -mol. The enzymic breakdown products
 of the alkyl and aryl **glucosinolates** were cytotoxic, but
 this activity was not affected by subsequent nitrite treatment.
 Given the levels at which indole **glucosinolates** occur in
 brassica vegetables, these findings suggest that their contribution
 to the observed mutagenic potential of these vegetables after
 nitrite treatment will be marginal. Further work is, however,
 needed to identify the exact chemical natures of both the N-nitroso
 compounds formed in nitrite-treated brassicas and their naturally
 occurring precursors.

L16 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on
 STN
 ACCESSION NUMBER: 1984:342461 BIOSIS
 DOCUMENT NUMBER: PREV198478078941; BA78:78941
 TITLE: PRELIMINARY STUDIES ON THE EFFECTS OF COPPER IRON AND
 MANGANESE IONS ON THE DEGRADATION OF 3 INDOLYLMETHYL
GLUCOSINOLATE A CONSTITUENT OF BRASSICA-SPP
 BY **MYROSINASE** EC-3.2.3.1.
 AUTHOR(S): SEARLE L M [Reprint author]; CHAMBERLAIN K; BUTCHER D
 N
 CORPORATE SOURCE: ROTHAMSTED EXPERIMENTAL STATION, HARPENDEN, HERTS AL5
 2JQ, UK

Searcher : Shears 571-272-2528

09/825989

SOURCE: Journal of the Science of Food and Agriculture,
(1984) Vol. 35, No. 7, pp. 745-748.
CODEN: JSFAAE. ISSN: 0022-5142.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB Cu (I and II) and Fe (II and III) ions had qualitatively similar effects on the degradation of radiolabeled 3-indolylmethylglucosinolate. In the presence of **myrosinase** they increased the production of 3-indolylacetonitrile (IAN) largely at the expense of ascorbigen (ASC). With the addition of these metal ions the ratio of IAN to the products of the alternative pathways (3,3'-diindolylmethane, ASC and formaldehyde) decreased as the pH increased from 4 to 7. These ions also led to a small increase in the non-enzymic production of IAN.

L16 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1983:233173 BIOSIS

DOCUMENT NUMBER: PREV198375083173; BA75:83173

TITLE: THE CONVERSION OF 3 INDOLYLMETHYL
GLUCOSINOLATE TO 3 INDOLYL
ACETONITRILE BY **MYROSINASE** AND ITS
RELEVANCE TO THE CLUBROOT DISEASE OF THE CRUCIFERAE.

AUTHOR(S): SEARLE L M [Reprint author]; CHAMBERLAIN K; RAUSCH T;
BUTCHER D N

CORPORATE SOURCE: ROTHAMSTED EXPERIMENTAL STATION, HARPENDEN, HERTS AL5
2JQ, UK

SOURCE: Journal of Experimental Botany, (1982) Vol. 33, No.
136, pp. 935-942.
CODEN: JEBOA6. ISSN: 0022-0957.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB [Methylene-14C]-3-indolylmethylglucosinolate (14C-IMG) was converted in vitro to [methylene-14C]-3-indolylacetonitrile (14C-IAN) by **myrosinase** [thioglucoside glucohydrolase EC 3.2.3.1] over a pH range of 4.0-6.0 and this conversion was enhanced by ferrous ions. Other products of the reaction included 3-indolylmethanol, 3,3'-diindolylmethane and ascorbigen A. Trace amounts of 14C-IAN were produced non-enzymically from 14C-IMG in the presence of ferrous ion over a similar pH range. Furthermore, swede tissues (Brassica napus cv. Danestone) infected with Plasmodiophora brassicae Woron. could convert 14C-IMG to 14C-IAN. These results were consistent with the hypothesis that the overgrowth symptoms of the clubroot disease are caused by the conversion of IMG to the auxin precursor IAN.

L16 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 5

ACCESSION NUMBER: 1980:200330 BIOSIS

DOCUMENT NUMBER: PREV198069075326; BA69:75326

TITLE: AN HIGH PRESSURE LIQUID CHROMATOGRAPHIC METHOD FOR
SIMULTANEOUS QUANTITATION OF INDIVIDUAL **ISO**
THIO CYANATES AND OXAZOLIDINETHIONE
IN **MYROSINASE** EC-3.2.3.1 DIGESTS OF

Searcher : Shears 571-272-2528

09/825989

RAPESEED MEAL.
 AUTHOR(S): MAHESHWARI P N [Reprint author]; STANLEY D W; GRAY J I; VOORT F R
 CORPORATE SOURCE: DEP FOOD SCI, UNIV GUELPH, GUELPH, ONT N1G 2W1, CAN
 SOURCE: Journal of the American Oil Chemists' Society, (1979)
 Vol. 56, No. 9, pp. 837-841.
 CODEN: JAOCA7. ISSN: 0003-021X.
 DOCUMENT TYPE: Article
 FILE SEGMENT: BA
 LANGUAGE: ENGLISH

AB A simple, rapid and precise method for simultaneous quantitation of individual **isothiocyanates** and oxazolidinethione in **myrosinase** digests of rapeseed meal has been developed. The method consists of inactivation of native **myrosinase** activity present in the seedmeal, followed by digestion with mustard **myrosinase** (thioglucoside glucohydrolase, EC 3.2.3.1) to hydrolyze rapeseed **glucosinolates** quantitatively to **isothiocyanates** and oxazolidinethione. These hydrolytic products are extracted in methylene chloride as soon as they are formed and finally resolved by a reverse phase high pressure liquid chromatography (HPLC) technique on a μ Bondapak C18 column using aqueous **acetonitrile** as solvent and an UV absorbance detector set at 254 nm. The lower limits of quantitation by this method in a single aliquot applied to the column were 0.2 μ g for the **isothiocyanates** and 0.01 μ g for the oxazolidinethione. Recoveries of allyl **isothiocyanate**, oxazolidinethione and sinigrin added to Brassica juncea, prior to digestion, were quantitative and averaged at 94.5, 93.0 and 91.2% with SD of 1.5, 3.3 and 2.8%, respectively. The butenyl and pentenyl **isothiocyanates** and oxazolidinethione in Tower (B. napus) and Candle (B. campestris) rapeseeds, and allyl **isothiocyanate** in B. juncea were the major hydrolytic products of **glucosinolates**. The identity of peaks corresponding to these compounds on a HPLC chromatogram was confirmed by mass spectroscopy.

L16 ANSWER 14 OF 16 MEDLINE on STN DUPLICATE 6
 ACCESSION NUMBER: 75153618 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 1127728
 TITLE: Aryl hydrocarbon hydroxylase induction in rat tissues by naturally occurring indoles of cruciferous plants.
 AUTHOR: Loub W D; Wattenberg L W; Davis D W
 SOURCE: Journal of the National Cancer Institute, (1975 Apr) 54 (4) 985-8.
 Journal code: 7503089. ISSN: 0027-8874.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 197507
 ENTRY DATE: Entered STN: 19900310
 Last Updated on STN: 19970203
 Entered Medline: 19750724

AB A phytochemical investigation to identify inducers of increased aryl hydrocarbon hydroxylase (AHH) activity from three cruciferous vegetables, Brussels sprouts, cabbage, and cauliflower, resulted in

Searcher : Shears 571-272-2528

09/825989

the identification of indole-3-acetonitrile, indole-3-carbinol, and 3,3'-diindolylmethane as naturally occurring inducers. These compounds are produced during the hydrolysis of indolyl-methyl **glucosinolate** by the plant enzyme **myrosinase**.

L16 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1974:169038 BIOSIS
DOCUMENT NUMBER: PREV197457068738; BA57:68738
TITLE: THE ROLE OF INDOLE **GLUCOSINOLATES** IN THE CLUB ROOT DISEASE OF THE CRUCIFERAE.
AUTHOR(S): BUTCHER D N; EL-TIGANI S; INGRAM D S
SOURCE: Physiological Plant Pathology, (1974) Vol. 4, No. 1, pp. 127-140.
CODEN: PPPYBC. ISSN: 0048-4059.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

L16 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1970:205651 BIOSIS
DOCUMENT NUMBER: PREV197051115651; BA51:115651
TITLE: INDOLE **ACETO NITRILE** SYNTHESIS FROM GLUCOBRASSICIN PH DEPENDENCE AND IMPORTANCE FOR GROWTH.
AUTHOR(S): SCHRAUDOLF H; WEBER H
SOURCE: Planta (Heidelberg), (1969) Vol. 88, No. 2, pp. 136-143.
CODEN: PLANAB. ISSN: 0032-0935.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

FILE 'CAPLUS' ENTERED AT 12:16:48 ON 24 JUN 2004

L17 1 S L4 AND (DMSO OR DMF)
L18 0 S L17 NOT L11

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CABA, AGRICOLA, FSTA, LIFESCI, CANCERLIT' ENTERED AT 12:17:15 ON 24 JUN 2004

L19 1 S L17
L20 1 S L19 NOT L15

L20 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:513019 BIOSIS
DOCUMENT NUMBER: PREV200300516359
TITLE: A facile and efficient synthesis of 14C-labelled sulforaphane.
AUTHOR(S): D'Souza, Christopher A.; Amin, Shantu; Desai, Dhimant [Reprint Author]
CORPORATE SOURCE: Institute for Cancer Prevention, 1 Dana Road, Valhalla, NY, 10595, USA
ddesai@ifcp.us

Searcher : Shears 571-272-2528

09/825989

SOURCE: Journal of Labelled Compounds and
Radiopharmaceuticals, (August 2003) Vol. 46, No. 9,
pp. 851-859. print.
ISSN: 0362-4803 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 5 Nov 2003

Last Updated on STN: 5 Nov 2003

AB **Isothiocyanates** have gained considerable attention for their role as potent chemopreventive agents. Sulforaphane, 1a (SFN), a naturally occurring **isothiocyanate**, was isotopically labelled in five steps starting from 3-(methylthio)-1-propanol (2). Reacting 2 with tosyl chloride in the presence of Et₃N yielded the tosylate 3. Gently refluxing 3 with K¹⁴CN in DMF gave the nitrile 4b. Reduction to the amine 5b was achieved using BH₃-THF. Oxidation with 30% hydrogen peroxide followed by treatment with thiophosgene yielded (+-)(1-¹⁴C)SFN, 1b. The overall radiochemical yield was 4.4% based on the starting K¹⁴CN.

(FILE 'CAPLUS' ENTERED AT 12:18:20 ON 24 JUN 2004)

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON ISOTHIOCYANATE/CN
L3 32844 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR ISOTHIOCYANATE OR
ISO(W) (THIOCYANATE OR THIO CYANATE) OR ISOTHIO CYANATE
OR GLUCOSINOLATE
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON "DIMETHYL SULFOXIDE"/CN
L6 2 SEA FILE=REGISTRY ABB=ON PLU=ON (ACETONITRILE/CN OR
"ACETONITRILE (13CH3CN)"/CN)
L7 1 SEA FILE=REGISTRY ABB=ON PLU=ON DIMETHYLFORMAMIDE/CN
L21 56709 SEA FILE=CAPLUS ABB=ON PLU=ON (L5 OR DIMETHYLSULFOXIDE
OR DIMETHYLSULPHOXIDE OR DI(W) (METHYLSULFOXIDE OR
METHYLSULPHOXIDE OR (ME OR METHYL) (W) (SULFOXIDE OR
SULPHOXIDE)) OR DIMETHYL(W) (SULFOXIDE OR SULPHOXIDE) OR
DMSO)
L22 4851 SEA FILE=CAPLUS ABB=ON PLU=ON L21 AND (L6 OR ACETONITRI
LE OR ACETO NITRILE)
L23 2784 SEA FILE=CAPLUS ABB=ON PLU=ON L22 AND (L7 OR DIMETHYLFO
RMAMIDE OR DI(W) (METHYLFORMAMIDE OR (ME OR METHYL) (W) FORM
AMIDE) OR DIMETHYL FORMAMIDE OR DMF)
L24 34 SEA FILE=CAPLUS ABB=ON PLU=ON L23 AND L3
L25 2 SEA FILE=CAPLUS ABB=ON PLU=ON L24 AND (EXTRACT? OR
EXT##)

L26 1 L25 NOT L11

L26 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1981:128527 CAPLUS

DOCUMENT NUMBER: 94:128527

TITLE: Anion solvation free energies from distribution
equilibriums

AUTHOR(S): Marcus, Y.; Pross, E.; Hormadaly, J.

CORPORATE SOURCE: Dep. Inorg. Anal. Chem., Hebrew Univ.,
Jerusalem, Israel

Searcher : Shears 571-272-2528

09/825989

SOURCE: Int. Solvent Extr. Conf., [Proc.] (1980), Volume 3, Paper 80-117, 8 pp.. Assoc. Ing. Univ. Liege: Liege, Belg.
CODEN: 45DZA9

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The solvation Gibbs free energies of anions (X-) are key items for understanding the solvent **extraction** equilibrium Transfer Gibbs free energies, $\Delta G^{\circ}(X-, W \rightarrow S)$, based on the tetraphenylarsonium tetraphenylborate [15627-12-0] assumption, represent them adequately. Data for these for 11 anions X- and 15 solvents S are tabulated, and expressed parametrically as $\Delta G^{\circ}(X-, W \rightarrow S) = a(X-) + b(X-)[ET(W) - ET(S)]$ in terms of the solvent polarity index ET. A distribution method, based on the sequestration of K+ by crown ethers, provides exptl. data for anion transfer between water and immiscible solvents, relevant to solvent **extraction** The equation used is $\Delta G^{\circ}(X-, W \rightarrow S) = -RT \ln K_{\text{distr}}(X-, S/W) + p(1/\epsilon S) + q$, where K is the equilibrium constant for the ion-pair **extraction** of $KCw+X$ (Cw is the crown ether), ϵS the dielec. constant, p an independently known constant, and q must be obtained by calibration with a solvent with known $\Delta Tg^{\circ}(X-, W \rightarrow S)$.

IT 67-68-5, properties 68-12-2, properties 75-05-8, properties
RL: PRP (Properties)
(free energy of transfer and anions from water to)

IT 302-04-5, properties
RL: PRP (Properties)
(free energy of transfer of, from water to solvent, solvation in relation to)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CABA, AGRICOLA, FSTA, LIFESCI, CANCERLIT' ENTERED AT 12:22:16 ON 24 JUN 2004)

L27 8 S L25

L28 1 S L27 NOT (L15 OR L19)

L28 ANSWER 1 OF 1 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998153219 EMBASE

TITLE: Solvent **extraction** of europium from aqueous-organic solutions by solvating **extractants**.

AUTHOR: Hala J.

CORPORATE SOURCE: J. Hala, Department of Inorganic Chemistry, Masaryk University, Kotlarska 2, 61137 Brno, Czech Republic

SOURCE: Journal of Radioanalytical and Nuclear Chemistry, (1998) 230/1-2 (135-141).
Refs: 21
ISSN: 0236-5731 CODEN: JRNCMD

COUNTRY: Hungary

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

Searcher : Shears 571-272-2528

09/825989

AB The partition of Eu(III) between benzene containing solvating **extractants** (TBP, TOPO, dioctylsulfoxide) and aqueous nitrate, perchlorate and thiocyanate solutions containing various organic solvents miscible with water (alcohols, acetone, **acetonitrile**, ethylene glycol, **dimethyl sulfoxide** and **dimethylformamide**) was investigated. Depending on the specific **extraction** system, the presence of organic solvents in the mixed phase showed various effects on the distribution ratio of Eu(III). These were discussed in terms of solute-solvent interactions. The results in the systems containing **dimethylformamide** and **dimethyl sulfoxide** indicated complexation of Eu(III) with these solvents in the polar phase.

FILE 'CAPLUS' ENTERED AT 12:27:04 ON 24 JUN 2004

L31 8 SEA ABB=ON PLU=ON L3 AND (THIOGLYCOSIDASE OR THIO
GLYCOSIDASE OR GLUCOSINOLASE)
L32 0 SEA ABB=ON PLU=ON L31 AND (L5 OR DIMETHYLSULFOXIDE OR
DIMETHYLSULPHOXIDE OR DI(W) (METHYLSULFOXIDE OR METHYLSULP
HOXIDE OR (ME OR METHYL) (W) (SULFOXIDE OR SULPHOXIDE)) OR
DIMETHYL(W) (SULFOXIDE OR SULPHOXIDE) OR DMSO)
L33 0 SEA ABB=ON PLU=ON L31 AND (L6 OR ACETONITRILE OR ACETO
NITRILE)
L34 0 SEA ABB=ON PLU=ON L31 AND (L7 OR DIMETHYLFORMAMIDE OR
DI(W) (METHYLFORMAMIDE OR (ME OR METHYL) (W) FORMAMIDE) OR
DIMETHYL FORMAMIDE OR DMF)

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
JICST-EPLUS, JAPIO, CABA, AGRICOLA, FSTA, LIFESCI, CANCERLIT'
ENTERED AT 12:28:24 ON 24 JUN 2004

L35 0 SEA ABB=ON PLU=ON L32
L36 1 SEA ABB=ON PLU=ON L33
L37 0 SEA ABB=ON PLU=ON L34
L38 0 SEA ABB=ON PLU=ON L36 NOT (L15 OR L19 OR L28)

(FILE 'MEDLINE' ENTERED AT 12:30:40 ON 24 JUN 2004)

L29 872 SEA FILE=MEDLINE ABB=ON PLU=ON ISOTHIOCYANATES/CT
L30 329 SEA FILE=MEDLINE ABB=ON PLU=ON GLUCOSINOLATES/CT
L43 1265 SEA FILE=MEDLINE ABB=ON PLU=ON ACETONITRILES/CT
L44 1061 SEA FILE=MEDLINE ABB=ON PLU=ON DIMETHYLFORMAMIDE/CT
L45 9846 SEA FILE=MEDLINE ABB=ON PLU=ON "DIMETHYL SULFOXIDE"/CT
L47 8 SEA FILE=MEDLINE ABB=ON PLU=ON (L29 OR L30) AND (L43
OR L44 OR L45)

L47 ANSWER 1 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2004070091 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14871576
TITLE: In vitro digestion of sinigrin and glucotropaeolin by
single strains of Bifidobacterium and identification
of the digestive products.
AUTHOR: Cheng D-L; Hashimoto K; Uda Y
CORPORATE SOURCE: Department of Bioproductive Sciences, Utsunomiya
University, 350 Minemachi, Utsunomiya, 321-8505
Japan.
SOURCE: Food and chemical toxicology : an international

Searcher : Shears 571-272-2528

09/825989

journal published for the British Industrial Biological Research Association, (2004 Mar) 42 (3) 351-7.
 Journal code: 8207483. ISSN: 0278-6915.

PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200404
 ENTRY DATE: Entered STN: 20040212
 Last Updated on STN: 20040407
 Entered Medline: 20040406

ED Entered STN: 20040212
 Last Updated on STN: 20040407
 Entered Medline: 20040406

AB Three strains of Bifidobacterium sp., B. pseudocatenulatum, B. adolescentis, and B. longum were studied for their ability to digest glucosinolates, sinigrin (SNG) and glucotropaeolin (GTL), in vitro. All strains digested both glucosinolates during 24-48 h cultivation, accompanied by a decline in the medium pH from 7.1 to 5.2. The digestion of glucosinolates by a cell-free extract prepared from sonicated cells of B. adolescentis, but not cultivated broth, increased in the presence of 0.5 mM l-ascorbic acid. Also, a time-dependent formation of allyl isothiocyanate (AITC) was observed when the cell-free extract was incubated with 0.25 mM SNG for 120 min at pH 7.0. These reaction features suggest that the digestive activity may have been due to an enzyme similar to myrosinase, an enzyme of plant origin. GC-MS analysis of the Bifidobacterial cultured broth showed that the major products were 3-butenenitrile (BCN) and phenylacetonitrile (PhACN), from SNG and GTL, respectively and nitriles, probably due to a decrease in the pH of the media. AITC and benzyl isothiocyanate (BzITC) were barely detectable in the broth. It was concluded that the three species of Bifidobacteria could be involved in digestive degradation of glucosinolates in the human intestinal tract.

L47 ANSWER 2 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 2000437676 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10869674
 TITLE: Supercritical fluid chromatography as a method of analysis for the determination of 4-hydroxybenzylglucosinolate degradation products.
 AUTHOR: Buskov S; Hasselstrom J; Olsen C E; Sorensen H; Sorensen J C; Sorensen S
 CORPORATE SOURCE: Chemistry Department, Royal Veterinary and Agricultural University, Thorvaldsensvej 40, DK-1871, Frederiksberg C, Denmark.
 SOURCE: Journal of biochemical and biophysical methods, (2000 Jul 5) 43 (1-3) 157-74.
 Journal code: 7907378. ISSN: 0165-022X.

PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200009
 ENTRY DATE: Entered STN: 20000928

Searcher : Shears 571-272-2528

09/825989

Last Updated on STN: 20000928

Entered Medline: 20000920

ED Entered STN: 20000928

Last Updated on STN: 20000928

Entered Medline: 20000920

AB In the present study analytical and preparative supercritical fluid chromatography (SFC) were used for investigation of myrosinase catalysed degradation of 4-hydroxybenzylglucosinolate (sinalbin). Sinalbin occurs as a major glucosinolate in seeds of *Sinapis alba* L., in various mustards and other food products. The degradation products were identified and quantified by analysis based on a developed SFC method using a bare silica column. Determinations comprised transformation products of sinalbin, produced both during degradation of isolated sinalbin, and during autolysis of meal from *S. alba* seeds. The conditions in the developed SFC method were used as basis for the preparative SFC procedure applied for isolation of the components prior to their identification by nuclear magnetic resonance (NMR) spectroscopy. Myrosinase catalysed sinalbin hydrolysis resulted in the reactive 4-hydroxybenzyl isothiocyanate as an initial product at pH values from 3.5 to 7.5 whereas 4-hydroxybenzyl cyanide was one of the major products at low pH values. 4-Hydroxybenzyl isothiocyanate was found to disappear from the aqueous reaction mixtures in a few hours, as it reacted easily with available nucleophilic reagents. 4-Hydroxybenzyl alcohol was found as the product from reaction with water, and with ascorbic acid, 4-hydroxybenzylascorbigen was produced.

L47 ANSWER 3 OF 8

MEDLINE on STN

ACCESSION NUMBER: 2000244162 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10782305

TITLE: Synthesis of 6,7-dideoxy-7-isothiocyanatoheptoses: stable fully unprotected monosaccharide isothiocyanates.

AUTHOR: Benito J M; Oriz Mellet C; Garcia Fernandez J M

CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Quimica, Universidad de Sevilla, Spain.

SOURCE: Carbohydrate research, (2000 Jan 12) 323 (1-4) 218-25.

Journal code: 0043535. ISSN: 0008-6215.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200007

ENTRY DATE: Entered STN: 20000720

Last Updated on STN: 20000720

Entered Medline: 20000710

ED Entered STN: 20000720

Last Updated on STN: 20000720

Entered Medline: 20000710

AB Methyl 6,7-dideoxy-7-isothiocyanato-alpha-D-glucopyranosides (manno) (galacto)-heptopyranosides have been synthesized in four steps by homologation of the respective methyl hexopyranosides via the corresponding heptopyranosyduronitriles. Neither intra- nor intermolecular thiocarbamate formation was observed, even under rather strenuous acidic or basic conditions. The reducing

Searcher : Shears 571-272-2528

09/825989

derivative 6,7-dideoxy-7-isothiocyanato-alpha-D-glucopyranose was also a stable compound in aqueous solution in the absence of base. Formation of a six-membered intramolecular cyclic thiocarbamate was achieved in DMF solution in the presence of triethylamine. The title compounds are the first examples of stable fully unprotected monosaccharide isothiocyanates.

L47 ANSWER 4 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 96193067 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 8610048
 TITLE: Selective toxicity of compounds naturally present in food toward the transformed phenotype of human colorectal cell line HT29.
 AUTHOR: Musk S R; Stephenson P; Smith T K; Stening P; Fyfe D; Johnson I T
 CORPORATE SOURCE: Agricultural and Food Research Council, institute of Food Research, Norwich Laboratory, UK.
 SOURCE: Nutrition and cancer, (1995) 24 (3) 289-98.
 Journal code: 7905040. ISSN: 0163-5581.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199605
 ENTRY DATE: Entered STN: 19960605
 Last Updated on STN: 19990129
 Entered Medline: 19960524

ED Entered STN: 19960605
 Last Updated on STN: 19990129
 Entered Medline: 19960524

AB It has previously been observed that allyl isothiocyanate, a compound naturally present in the diet, is more cytotoxic toward the human colorectal adenocarcinoma cell line HT29 in its control transformed state than after exposure to sodium butyrate or to dimethylformamide, which slow growth and induce differentiation (detransformation). In the present study, a range of other dietary compounds were assayed for such selective toxicity. These compounds were chosen as constituents of foodstuffs that have been identified from epidemiologic studies as being potentially antitumorigenic and also as having anticarcinogenic activity in experimental models. Benzyl and phenethyl isothiocyanate, benzyl thiocyanate, and quercetin showed decreased toxicity towards HT29 after detransformation of the cells by one or both treatments, whereas no change was observed in the sensitivity to diallyl sulfide or diallyl disulfide. It is proposed that the presence of such selectively toxic compounds in the diet may inhibit the development of tumors by interfering with the growth of preneoplastic lesions while having little effect on normal cells. The cumulative effects of these inhibitions may contribute to the chemopreventive properties of the parent foodstuffs observed in epidemiologic studies.

L47 ANSWER 5 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 94037293 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 8222057
 TITLE: Allyl isothiocyanate is selectively toxic to transformed cells of the human colorectal tumour line

Searcher : Shears 571-272-2528

09/825989

HT29.
 AUTHOR: Musk S R; Johnson I T
 CORPORATE SOURCE: AFRC Institute of Food Research, Norwich Laboratory,
 Norwich Research Park, Colney, Norfolk, UK.
 SOURCE: Carcinogenesis, (1993 Oct) 14 (10) 2079-83.
 Journal code: 8008055. ISSN: 0143-3334.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199312
 ENTRY DATE: Entered STN: 19940117
 Last Updated on STN: 19990129
 Entered Medline: 19931201

ED Entered STN: 19940117
 Last Updated on STN: 19990129
 Entered Medline: 19931201

AB Allyl isothiocyanate, a constituent of mustard and certain vegetables found in the human diet, was tested for cytotoxic and cytostatic effects in HT29 human colon carcinoma cells in vitro. For an exposure time of 24 h, allyl isothiocyanate exhibited a Dq of 0.32 microgram/ml and a D0 of 0.74 micrograms/ml. Following detransformation of the cells by treatment with sodium butyrate or dimethylformamide the cells became more resistant to the cytotoxic effects of allyl isothiocyanate, the Dq increasing to 0.74 microgram/ml and the D0 to 0.96 microgram/ml (with butyrate) or 0.84 microgram/ml (with dimethylformamide). At the Dq value for detransformed cells the survival of the control cells was reduced to 56%. Allyl isothiocyanate was also found to be less cytostatic to the mass growth of detransformed populations in that daily doses of 1.6 micrograms/ml over a week reduced the final number of detransformed cells relative to untreated cultures by < 25% whilst growth of the transformed cultures was reduced by > 60%. Given this increased sensitivity of the cells to allyl isothiocyanate when in the transformed state, it is hypothesized that, when consumed in the human diet, this compound may protect against the development of colorectal cancer by selectively inhibiting the growth of transformed cell clones within the gastrointestinal mucosa.

L47 ANSWER 6 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 92098517 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 1757417
 TITLE: A new approach to the study of glucosinolates by isocratic liquid chromatography. Part I. Rapid determination of desulfated derivatives of rapeseed glucosinolates.
 AUTHOR: Quinsac A; Ribaillier D; Elfakir C; Lafosse M; Dreux M
 CORPORATE SOURCE: Centre Technique Interprofessionnel des Oleagineux Metropolitains, Ardon, France.
 SOURCE: Journal - Association of Official Analytical Chemists, (1991 Nov-Dec) 74 (6) 932-9.
 Journal code: 7505559. ISSN: 0004-5756.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English

Searcher : Shears 571-272-2528

09/825989

FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199202
 ENTRY DATE: Entered STN: 19920223
 Last Updated on STN: 19980206
 Entered Medline: 19920206

ED Entered STN: 19920223
 Last Updated on STN: 19980206
 Entered Medline: 19920206

AB Liquid chromatographic (LC) analysis of desulfated derivatives of rapeseed glucosinolates has been carried out under isocratic elution conditions with different CN-bonded stationary phases. The effects of the eluant composition (water, acetonitrile, and methanol) with the stationary phase (Zorbax CN, Lichrospher CN, and Ultrasphere CN) and temperature (20 and 50 degrees C) are described. An isocratic LC method performed at room temperature using a Lichrospher CN column and water as mobile phase is proposed. The chromatographic analysis can be done in less than 12 min, and it is easier and less expensive than the traditional gradient mode. Four commercial samples of rapeseed containing various quantities of other cruciferous seeds (wild mustard and stinkweed) as an admixture have been analyzed to determine the total glucosinolate content. Relative standard deviations of repeatability of the isocratic and gradient LC methods ranged from 0.4 to 1.7% and from 2.7 to 4.7%, respectively. Comparison of the results showed good agreement between the 2 methods (better than 98%).

L47 ANSWER 7 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 88272993 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 3391960
 TITLE: Characterization of benzyl isothiocyanate and phenyl acetonitrile from papayas by mass spectrometry.
 AUTHOR: Cairns T; Siegmund E G; Stamp J J; Jacobs R M
 CORPORATE SOURCE: Food and Drug Administration, Office of Regulatory Affairs, Los Angeles, CA 90015.
 SOURCE: Journal - Association of Official Analytical Chemists, (1988 May-Jun) 71 (3) 547-50.
 Journal code: 7505559. ISSN: 0004-5756.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198808
 ENTRY DATE: Entered STN: 19900308
 Last Updated on STN: 19900308
 Entered Medline: 19880825

ED Entered STN: 19900308
 Last Updated on STN: 19900308
 Entered Medline: 19880825

AB Two unidentified analytical responses in a papaya extract were structurally determined by mass spectrometry to be benzyl isothiocyanate and phenyl acetonitrile. Both these compounds have previously been shown to result from degradation of benzylglucosinolate that occurs naturally in the seeds of the fruit. Characterization by mass spectrometry has now provided a convenient mechanism to detect both these degradation compounds in extracts resulting from routine pesticide residue analysis.

Searcher : Shears 571-272-2528

09/825989

L47 ANSWER 8 OF 8 MEDLINE on STN
 ACCESSION NUMBER: 86180719 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 3961819
 TITLE: Glutathione- and cysteine-mediated cytotoxicity of allyl and benzyl isothiocyanate.
 AUTHOR: Bruggeman I M; Temmink J H; van Bladeren P J
 SOURCE: Toxicology and applied pharmacology, (1986 Apr) 83 (2) 349-59.
 Journal code: 0416575. ISSN: 0041-008X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198604
 ENTRY DATE: Entered STN: 19900321
 Last Updated on STN: 20000303
 Entered Medline: 19860430

ED Entered STN: 19900321
 Last Updated on STN: 20000303
 Entered Medline: 19860430

AB Allyl isothiocyanate has been reported to be a bladder carcinogen in male rats. On the other hand, benzyl isothiocyanate is an anti-carcinogen. These contradicting properties led us to investigate the cytotoxicity of these compounds in RL-4 rat hepatocytes. Since conjugation with glutathione plays an important role in the metabolism of these isothiocyanates, the glutathione and L-cysteine derivatives were also tested for cytotoxicity (electron microscopy, trypan blue exclusion, cell attachment, and inhibition of cell division). Both types of conjugates caused considerable toxicity: allyl isothiocyanate conjugates gave effects comparable to the parent compound, but benzyl isothiocyanate was more toxic than its conjugates. Addition of excess glutathione (greater than 4mM) to the free isothiocyanates as well as their conjugates abolished cytotoxicity up to the highest concentration tested (250 microM). Addition of excess L-cysteine (5 to 20 mM) lowered the effects but did not abolish them. The reaction of thiols with isothiocyanates was readily reversible: 15 min after dissolving the conjugates in buffer, pH 7.4, an equilibrium was established in which 9 to 15% of the conjugates was converted to free isothiocyanate. Two hours after addition of 1 mM of the L-cysteine conjugates to medium containing 5 mM glutathione, 80% of the total conjugates was present as the glutathione derivatives. The glutathione conjugates were similarly converted to L-cysteine conjugates. Glutathione conjugates are not able to enter the cell, thus their toxicity is presumably due to the release of free isothiocyanate, and in the presence of excess glutathione no toxicity was observed. L-cysteine derivatives are able to cross the cell membrane, thus excess L-cysteine diminishes cytotoxicity, since less free isothiocyanate is present outside the cells, but does not completely protect the cells. Glutathione and cysteine can be regarded as transporting agents for the isothiocyanates through the body. Initial detoxification can be followed by release of the reactive compound at some other site.

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Searcher : Shears 571-272-2528

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FILE 'HOME' ENTERED AT 12:35:27 ON 24 JUN 2004

Searcher : Shears 571-272-2528

5-H16



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 125487

To: Cybille Delacroix
Location: REM-4C85&4C70
Art Unit: 1641
Friday, June 25, 2004

Case Serial Number: 09/875989

From: Beverly Shears
Location: Remsen Bldg.
RM 1A54
Phone: 571-272-2528

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Search Notes

SA 28





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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,989	04/05/2001	Jed W. Fahey	046585/0138	4463

22428 7590 01/27/2005

FOLEY AND LARDNER
 SUITE 500
 3000 K STREET NW
 WASHINGTON, DC 20007

EXAMINER

DELACROIX MUIRHEI, CYBILLE

ART UNIT	PAPER NUMBER
----------	--------------

1614

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary**Application No.**

09/825,989

Applicant(s)

FAHEY ET AL.

Examiner

Cybille Delacroix-Muirheid

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-71 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 48-57 is/are allowed.
- 6) ☒ Claim(s) 58-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 05/22/2002.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Application/Control Number: 09/825,989
Art Unit: 1614

Page 2

Detailed Action

The following is responsive to Applicant's amendment received Jan. 20, 2004.

Claims 1-47 are cancelled. No new claims are added. Claims 48-71 are currently pending.

The previous objection of claim 58 on page 2 of the office action mailed Nov. 19, 2003 is withdrawn in view of Applicant's amendment and the remarks contained therein.

Upon further consideration of the pending claims and specification, the following new ground of rejection is respectfully submitted.

The indication of allowability of claims 59-71 is withdrawn. Prosecution on the merits is reopened.

Claims 48-57 remain allowable over the prior art.

New Ground(s) of Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 58-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation "**high** concentration of glucosinolates and isothiocyanates " in these claims is a relative term which renders the claims indefinite. The expression "high concentration" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Application/Control Number: 09/825,989
Art Unit: 1614

Page 3

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all of the criteria for patentability and whether the specification meets the criteria of 35 USC 112, first paragraph with respect to the claimed invention." Please see MPEP 2173.

Because the limitation "high concentration" would invite subjective interpretations of whether or not a particular plant tissue was included by or excluded from the present claims, the Examiner respectfully submits that the public would not be informed of the boundaries of what constitutes infringement of the present claims and thus the claims do not meet the requirements of 35 USC 112, second paragraph.

Conclusion

Claims 58-71 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone

Application/Control Number: 09/825,989
Art Unit: 1614


Page 4

number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM

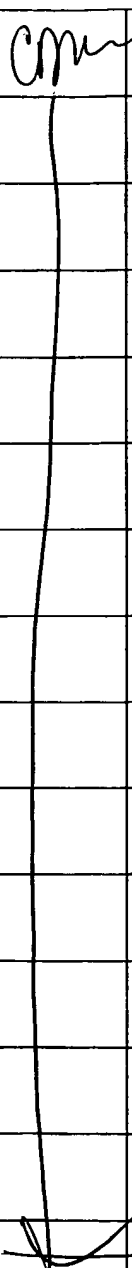
Jan. 24, 2005


RAYMOND HENLEY III
PRIMARY EXAMINER
AU 1614

Form PTO-1449 (MODIFIED)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 046585/0138		SERIAL NO. <u>09/825,989</u> <u>Unassigned</u>		
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				APPLICANT Jed FAHEY et al.				
				FILING DATE April 5, 2001		GROUP ART UNIT <u>1614</u> <u>Unassigned</u>		
U.S. PATENT DOCUMENTS								
EXAMINER INITIAL	REF	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE IF APPROPRIATE	
<i>Cmm</i>	A1	5,725,895	3/98	Fahey et al.	426	49		
<i>Cmm</i>	A2	4,511,988 5,411,986	5/86 5/95	Cho et al.	514	514		
FOREIGN PATENT DOCUMENTS								
	REF	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION	
							YES	NO
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)								
	A3	The Sproutletter, Number 25, Nov. - Dec. 1984.						
<i>Cmm</i>	A4	"The Sproutletter" May-June 1981, No. 4.						
<i>Cmm</i>	A5	Roy Bruder, Ph.D., Discovering Natural Foods, (including pgs.203-209), Woodbridge Press, 1982.						
	A6	Brian R. Clement, Hippocrates Health Program, (including pgs 7-11), Hippocrates Publications, 1989.						
	A7	Jethro Kloss, The Back to Eden Cookbook, pgs. 61-61, Woodbridge Press, 1974.						
EXAMINER <i>Cmm</i>				DATE CONSIDERED 5-15-02 1-23-05				
* EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include any copy of this form with next communication to applicant.								

Form PTO-1449 (MODIFIED)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 046585/0138		SERIAL NO. Unassigned	
INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i>				APPLICANT Jed FAHEY et al.			
				FILING DATE April 5, 2001		GROUP ART UNIT Unassigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
cm	A8	Steve Meyerowitz, Sproutmann Kitchen Garden Cookbook, The Sprouthouse, Inc., pgs. 178-179, 290, 1994.					
J	A9	Steve Meyerowitz, Sprout It, One week from Seed to Salad, The Sprouthouse, Inc., (including pgs. 84-85, 120-123), June 1994.					
J	A10	Steve Meyerowitz, The Complete Guide to Sprouting, Sprouts The Miracle Food, Sproutman Publications, (including pgs. 121-2), May 1998.					
	A11	Esther Munroe, Sprouts to Grow and Eat, (including pgs. 2-15), Dec. 1974.					
cm	A12	Jean Hewitt, The New York Times "New Natural Foods Cookbook", Avon Books, pgs. 200-203, 1982.					
J	A13	Martha H. Oliver, Add a Few Sprouts To Eat Better for Less Money, Pivot Original Health Books, (including pgs. 52-53, 118-119), 1975.					
	A14	James C. Schmidt, Horticulture Facts, "Growing Sprouts Indoors", (Rev. 4/81).					
	A15	Angnes Toms, The Joy of Eating Natural Foods, The Complete Organic Cookbook, pgs. 318-319, Nov. 1971.					
	A16	Karen Cross Whyte, The Complete Sprouting Cookbook, Troubador Press, (including pgs. 57-59), 1973.					
	A17	Ann Wigmore, The Sprouting Book, Avery Publications, (including pgs. 29-37), 1986.					
	A18	Debra Schwarze, Growing Sprouts, Neb Guide, Jan. 1989.					
	A19	John Tobe, Sprouts Elixir of Life", 1970.					
	A20	Alicia Bay Laurel, "Living on the Earth" a Vintage Book.					
J	A21	David Ehrlich with George Wolf, Foreward by Peter Albright, M.D., "The Bowell Book", Schocken Books, 1981.					
J	A22	"The Good News Sprouts Recipe Book" ISGA, Aug. 1992.					

Form PTO-1449 (MODIFIED)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 046585/0138		SERIAL NO. Unassigned	
INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i>				APPLICANT Jed FAHEY et al.			
				FILING DATE April 5, 2001		GROUP ART UNIT Unassigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
	A23	Ann Wigmore, "The Hippocrates Diet and Health Program", Avery Publications, 1984.					
	A24	Sprouting Publications Oahspe Foundation, Health and Sprouting Supplies.					
	A25	Sproutletter, #41, Summer, 1989.					
	A26	The Sproutletter, Number 27, March-April 1985.					
	A27	Steve Meyerowitz, Growing Vegetables Indoors", 1983.					
	A28	The Sproutletter, Number 24, Sept.-Oct. 1984.					
	A29	The Sproutletter, Issue 33, Spring 1987.					
	A30	The Sproutletter, Number 28, May-June 1985.					
	A31	The Sproutletter, Number 26, Jan-Feb 1985.					
	A32	Sprouting Publications, Health and Sprouting Supplies.					
	A33	The Sproutletter, Number 29, July - August 1985.					
	A34	Sproutletter, #40, Spring, 1989.					
	A35	The Sproutletter, Number 32, Summer.					
	A36	Sproutletter, #44, March 1991.					
	A37	Sproutletter, #36, Winter, 1987-88.					

Form PTO-1449 (MODIFIED)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 046585/0138		SERIAL NO. Unassigned	
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				APPLICANT Jed FAHEY et al.			
				FILING DATE April 5, 2001		GROUP ART UNIT Unassigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
	A38	Sproutletter, #39, Fall, 1988.					
	A39	Sproutletter, #43, May/June 1990.					
	A40	Sproutletter, #38, Summer, 1988.					
	A41	Sprouting Publications Health and Sprouting Supplies.					
	A42	Spring Sale for Members Only.					
	A43	The Sproutletter, A newsletter of useful and unusual information on sprouts, raw foods and nutrition.					
	A44	The Sproutletter, #31, Winter.					
	A45	Deirdre Purdy, ed., The Summer Kitchen, A Farmers' Market Cookbook, 1981.					
	A46	Viktoras Kulvinskis, M.S. Co-Director Hippocrates Health Institute, "Love Your Body or how to be a live food lover", 1974.					
	A47	The Sprout House Article from Newspaper.					
	A48	New Prices – New Products, July 1985 order form.					
	A49	Steve Meyerowitz, Indoor Vegetable Kit, The Sprout House.					
	A50	The Sprout House Newsletter, Issue #15, August, 1992.					
	A51	Sproutman's Exotic Seeds for Sprouting 100% Organically Grown Order Form.					
	A52	Complaint for Patent Infringement (Brassica Protection Products, LLC v. The Sproutman, Inc. dated September 20, 1999.					

Form PTO-1449 (MODIFIED)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 046585/0138		SERIAL NO. Unassigned	
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				APPLICANT Jed FAHEY et al.			
				FILING DATE April 5, 2001		GROUP ART UNIT Unassigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
cm	A53	Murry Tizer's Answer, Affirmative Defenses and Counterclaims dated June 28, 1999					
	A54	The Sproutman, Inc.'s Answer, Affirmative Defenses and Counterclaims dated June 28, 1999					
	A55	Request for Reexamination of U.S. Patent No. 5,725,895 filed October 11, 1999					
cm	A56	Sprout it! One Week From Seed to Salad, Steve Meyerowitz (The Sprout House, Inc., Great Barrington, MA), Pages 20-21, 58, 85-86, 120-123, 1983					
	A57	Munroe, E., Sprouts to Grow and Eat, the Steven Greene Press, (1974), pp. 2-9 and 14-15					
	A58	Schmidt, James C., Growing Sprouts Indoors, Cooperative Extension Service of the University of Illinois at Urbana-Champaign, College of Agriculture (1984) (pamphlet)					
cm	A59	Why? K.C., The Complete Sprouting Cookbook, Troubador Press (1983), pp 10-16, 57-60					
	A60	The Sprout House cookbook, Steve Meyerowitz (The Sprout House, Inc. Great Barrington, MA 1983), pages 20-21, 85, 120-123.					
	A61	The Good New Sprouts Recipe Book, International Sprout Growers Association, pp. 1-8, August 1992.					
cm	A62	Posner et al., "Design and Synthesis...and potency as Inducers of Anticarcinogenic Detoxication Enzymes", Journal of Medicinal Chemistry, Vol. 37, No. 1, pp. 170-175, 1994					
	A63	Zhang et al., "A major inducer of Anticarcinogenic protective enzymes from broccoli; isolation And education of structure", Proc. Natl. Acad. Sci. USA, Vol. 89, pp. 2399-2403, March 1992.					
	A64	Prochaska et al. "Rapid detective of inducers of enzymes that protect against carcinogens", Proc. Nat'l. Sci. USA Vol. 89, pp. 2394-2388, March 1992					
cm	A65	Zhang et al., "Anticarcinogenic activities of sulforaphane and structurally related synthetic norbornyl isothiocyanates", Proc. Natl. Sci. USA, Vol. 91, pp. 3147-3150, April 1994.					
	A66	Prochaska et al., "Regulatory Mechanisms of Monofunctional and Bifunctional Anticarcinogenic Enzyme, Inducers in Murine Liver,; Cancer Research Vol. 48, pp. 4776-4782, September 1988.					

Form PTO-1449 (MODIFIED)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO. 046585/0138		SERIAL NO. Unassigned	
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				APPLICANT Jed FAHEY et al.			
				FILING DATE April 5, 2001		GROUP ART UNIT Unassigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
Cm	A67	Prochaska et al., "Direct Measurement of NAD(P)H: Quinone Reductase from Cells Cultured in Microtiter Wells: A Screening Assay for...Inducers", analytical Biochemistry, Vol. 169, pp. 328-336, 1988.					
	A68	Beecher, "Cancer prevention properties of varieties of Brassica oleracea: a review 1-3 ", Am J. Clin. Nutr.: 59 (suppl.) pp. 1166 s-1170s, 1994.					
↓	A69	Prester et al., "Chemical and molecular regulation of enzymes that detoxify carcinogens", Proc. Natl. Acad. Sci. USA, Vol. 90, pp. 2965-2969, April 1993.					
	A70	Zhang et al., "Anticarcinogenic Activities of Organic Isothiocyanates: Chemistry and Mechanisms", Cancer Research suppl., 54, pp. 1976s-1981s, April 1, 1994.					
↓	A71	Tatalay, "The role of Enzyme Induction in Protection Against Carcinogenesis", Cancer Chemoprevention, pp. 469-478, 1992.					
	A72	Prester et al., "The Electrophile Counterattack Response: Protection Against Neoplasia and Toxicity", Advan. Enzyme Regul., vol. 33, pp. 281-296, 1993.					
↓	A73	Masilungan et al., "Screening of Philippine Medicinal Plants for Anticancer Agents using CCNSC "Protocols", Cancer Chemotherapy Reports (Part 2) Vol. 2, No.1, pp. 135-140, April 1971.					
	A74	Polasa et al., "Cancer preventive properties of varieties of Brassica oleracea: A review Source", American Journal of Clinical Nutrition 59 (5 Suppl), 1994.					
↓	A75	Patent Abstract of Japan Sect. No. 305, Vol. 9, No. 2371, p.2, September 1985.					
	A76	Barrett et al., "Protective Effect of Cruciferous Seed Meals Against Mouse Colon Cancer", Cereal Foods World 613, Vol. 39, No. 8, pp. 613, August 1994.					
EXAMINER				DATE CONSIDERED			
Cm				1-23-05			
* EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include any copy of this form with next communication to applicant.							



UNITED STATES PATENT AND TRADEMARK OFFICE

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BIBDATASHEET**CONFIRMATION NO. 4463**

Bib Data Sheet

SERIAL NUMBER 09/825,989	FILING DATE 04/05/2001 RULE	CLASS 514	GROUP ART UNIT 1614	ATTORNEY DOCKET NO. 046585/0138
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APPLICANTS

Jed W. Fahey, Eldersburg, MD;

Paul Talalay, Baltimore, MD;

**** CONTINUING DATA *******

This application is a DIV of 09/425,890 10/25/1999 PAT 6,242,018
 which is a DIV of 09/118,867 07/20/1998 PAT 6,177,122
 which is a DIV of 08/840,234 04/11/1997 PAT 5,968,567

**** FOREIGN APPLICATIONS *******

IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** SMALL ENTITY **

** 05/30/2001

Foreign Priority claimed 35 USC 119 (a-d) conditions met Verified and Acknowledged	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> Met after Allowance Examiner's Signature _____ Initials _____	STATE OR COUNTRY MD	SHEETS DRAWING 2	TOTAL CLAIMS 20	INDEPENDENT CLAIMS 2
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ADDRESS

22428
 FOLEY AND LARDNER
 SUITE 500
 3000 K STREET NW
 WASHINGTON , DC
 20007

TITLE

Cancer chemoprotective food products

FILING FEE RECEIVED 391	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	<input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____
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ISSUE SLIP STAPLE AREA (for additional cross references)

POSITION	INITIALS	ID NO.	DATE
FEE DETERMINATION			
O.I.P.E. CLASSIFIER			
FORMALITY REVIEW	AK	931	08/30/01
RESPONSE FORMALITY REVIEW			

INDEX OF CLAIMS

✓ Rejected N Non-elected
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 - (Through numeral) ... Canceled A Appeal
 + Restricted O Objected

165/1931

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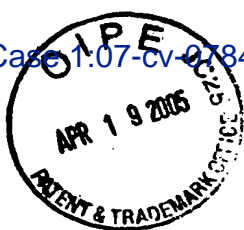
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	431	↓	↓
	615	↓	↓
updated		1/9/03	cm
updated		11/16/03	cm
updated		1-23-05	cm

INTERFERENCE SEARCHED

Class	Sub.	Date	Exmr.

SEARCH NOTES
(INCLUDING SEARCH STRATEGY)

	Date	Exmr.
EAST	5/1/02	cm
(search history in file)	↓	↓
EAST update	1/9/03	cm
EAST update	11/16/03	cm
search update reviewed library search	1-23-05	cm
	↓	↓



Atty. Dkt. No. 046585-0138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICEApplicant: Jed FAHEY *et al.*Title: CANCER CHEMOPROTECTIVE
FOOD PRODUCTS

Appl. No.: 09/825,989

Filing Date: 4/5/2001

Examiner: Cybille Delacroix-Muirheid

Art Unit: 1614

AMENDMENT AND REPLY UNDER 37 CFR § 1.111Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This communication is responsive to the Non-Final Office Action dated January 27, 2005, concerning the above-referenced patent application.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this document.

Remarks/Arguments begin on page 5 of this document.

Please amend the application as follows:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-47. (Canceled).

Claim 48. (Previously Presented): A method of extracting glucosinolates and isothiocyanates from plant tissue comprising homogenizing said plant tissue in an excess of a mixture of dimethyl sulfoxide, acetonitrile and dimethylformamide at a temperature sufficient to inactivate myrosinase enzyme activity.

Claim 49. (Previously Presented): The method of claim 48, wherein the ratio of dimethyl sulfoxide:acetonitrile:dimethylformamide is 1:1:1.

Claim 50. (Previously Presented): The method of claim 48, wherein said temperature is between 0°C and the freezing temperature of the extraction mixture.

Claim 51. (Previously Presented): The method of claim 48, wherein said temperature is between -50°C and the freezing temperature of the extraction mixture.

Claim 52. (Previously Presented): The method of claim 48, wherein said plant tissue is rich in glucosinolates.

Claim 53. (Previously Presented): The method of claim 52, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants or plant parts.

Claim 54. (Previously Presented): The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 55. (Previously Presented): The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 300,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 56. (Previously Presented): The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 400,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 57. (Previously Presented): The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 500,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 58. (Currently Amended): A method of making a food product comprising extracting glucosinolates and isothiocyanates from plant tissue having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential ~~a high concentration of glucosinolates and isothiocyanates~~, recovering said glucosinolates and isothiocyanates and adding said glucosinolates and isothiocyanates to food;

wherein said extracting comprises contacting said plant tissue with a non-toxic solvent at a temperature sufficient to inactivate myrosinase enzyme activity.

Claim 59. (Previously Presented): The method according to claim 58, wherein said solvent is water.

Claim 60. (Previously Presented): The method of claim 59, wherein said water is 100°C.

Claim 61. (Previously Presented): The method according to claim 58, wherein said solvent is liquid carbon dioxide.

Claim 62. (Previously Presented): The method according to claim 58, wherein said solvent is ethanol.

Claim 63. (Previously Presented): The method of claim 58, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants and plant parts.

Claim 64. (Cancelled).

Atty. Dkt. No. 046585-0138

Claim 65. (Previously Presented): The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 300,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 66. (Previously Presented): The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 400,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 67. (Previously Presented): The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 500,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Claim 68. (Previously Presented): The method of claim 58 wherein said food product is selected from the group consisting of a bread, a drink, a soup, a salad, a sandwich and a cereal.

Claim 69. (Previously Presented): The method of claim 68 wherein said drink is a tea.

Claim 70. (Previously Presented): The method of claim 58 wherein said extracting further comprises homogenizing said plant tissue with said non-toxic solvent.

Claim 71. (Previously Presented): The method of claim 63 wherein said sprouts, seeds, plants or plant parts have at least 250,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

Atty. Dkt. No. 046585-0138

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. This amendment changes and deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claim 64 is cancelled. Claim 58 is currently being amended. No claims are added. After amending the claims as set forth above, claims 48-63 and 65-71 are currently pending in this application.

The Examiner rejected claims 58-71 under 35 U.S.C. § 112, ¶ 2, asserting that the phrase "high concentration" found in claim 58 is indefinite. Without acquiescing in the rejection and without intending to abandon claimed subject matter but to expedite allowance, claim 58 is amended to incorporate the numerical limitation found in claim 64. In addition, claim 64 is now cancelled. Applicants respectfully submit that claims 58-63 and 65-71 are clear and that the public is informed of the boundaries of the claims. Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Atty. Dkt. No. 046585-0138

Respectfully submitted,

Date April 19, 2005

By Richard C. Peet

FOLEY & LARDNER LLP

Customer Number: 22428

Telephone: (202) 672-5483

Facsimile: (202) 672-5399

Richard C. Peet

Attorney for Applicant

Registration No. 35,792



Atty. Dkt. No. 046585-0138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jed FAHEY et al.

Title: CANCER CHEMOPROTECTIVE
FOOD PRODUCTS

Appl. No.: 09/825,989

Filing Date: 4/5/2001

Examiner: Cybille Delacroix-Muirheid

Art Unit: 1614

AMENDMENT TRANSMITTALMail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Transmitted herewith is an amendment in the above-identified application.

[X] Small Entity status under 37 C.F.R. § 1.9 and § 1.27 has been established by a previous assertion of Small Entity status.

[X] The fee required for additional claims is calculated below:

	Claims As Amended		Previously Paid For		Extra Claims Present		Rate		Additional Claims Fee
Total Claims:	23	-	24	=	0	x	\$50.00	=	\$0.00
Independent Claims:	2	-	3	=	0	x	\$200.00	=	\$0.00
First presentation of any Multiple Dependent Claims:						+	\$360.00	=	\$0.00
CLAIMS FEE TOTAL								=	\$0.00

Appl. No. 09/825,989
Atty. Dkt. No. 046585-0138

- ☐ Applicant hereby petitions for an extension of time under 37 C.F.R. §1.136(a) for the total number of months checked below:

<input type="checkbox"/> Extension for response filed within the first month:	\$120.00	\$0.00
<input type="checkbox"/> Extension for response filed within the second month:	\$450.00	\$0.00
<input type="checkbox"/> Extension for response filed within the third month:	\$1,020.00	\$0.00
EXTENSION FEE TOTAL:		\$0.00
<input type="checkbox"/> Statutory Disclaimer Fee under 37 C.F.R. 1.20(d):	\$130.00	\$0.00
CLAIMS, EXTENSION AND DISCLAIMER FEE TOTAL:		\$0.00
<input checked="" type="checkbox"/> Small Entity Fees Apply (subtract ½ of above):		\$0.00
TOTAL FEE:		\$0.00

- ☒ No fee is due.

- ☒ The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date 4/18/05

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5483
Facsimile: (202) 672-5399

By Richard C. Peet /for
Reg No 51113

Richard C. Peet
Attorney for Applicant
Registration No. 35,792

PATENT APPLICATION FEE DETERMINATION RECORD

Effective October 1, 2000

Application or Docket Number

09/825,989

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS	20	
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	20 minus 20 =	0
INDEPENDENT CLAIMS	2 minus 3 =	0
MULTIPLE DEPENDENT CLAIM PRESENT		<input type="checkbox"/>

SMALL ENTITY
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RATE	FEE		RATE	FEE
BASIC FEE	355.00	OR	BASIC FEE	710.00
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* If the difference in column 1 is less than zero, enter "0" in column 2

CLAIMS AS AMENDED - PART II

	(Column 1)	(Column 2)	(Column 3)
AMENDMENT A	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA
Total	24	Minus 4	= 4
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AMENDMENT B	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA
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AMENDMENT C	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA
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* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

CLAIMS ONLY							Application Number 09/825,989		Filing Date	
							Applicant(s)			
							* May be used for additional claims or amendments			
CLAIMS	AS FILED 4.19.05		AFTER FIRST AMENDMENT		AFTER SECOND AMENDMENT					
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L1	19617	dimethyl near2 (sulfoxid\$2 or sulphoxid\$2) and acetonitril\$3 and dimethylformamid\$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/08 19:06
L2	15802	dimethyl near2 (sulfoxid\$2 or sulphoxid\$2) and acetonitril\$3 and dimethylformamid\$3 and extract\$4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/08 19:07
L3	15772	dimethyl adj (sulfoxid\$2 or sulphoxid\$2) and acetonitril\$3 and dimethylformamid\$3 and extract\$4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/08 19:07
L4	5368	dimethyl adj (sulfoxid\$2 or sulphoxid\$2) same acetonitril\$3 same dimethylformamid\$3 and extract\$4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/08 19:08
L5	4208	dimethyl adj sulfoxid\$2 same acetonitril\$3 same dimethylformamid\$3 and extract\$4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/08 19:08
L6	247	dimethyl adj sulfoxid\$2 same acetonitril\$3 same dimethylformamid\$3 same extract\$4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/08 19:08

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	379	(dimethyl adj sulfoxid\$2 or DMSO) same acetonitril\$3 same dimethylformamid\$3 same extract\$5	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/11 12:00
L2	161	1 and @AY<="1997"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/07/11 12:00



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,989	04/05/2001	Jed W. Fahey	046585/0138	4463

22428 7590 07/14/2005

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EXAMINER

DELACROIX MUIRHEI, CYBILLE

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/825,989

Applicant(s)

FAHEY ET AL.

Examiner

Cybille Delacroix-Muirheid

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2005.
 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-63 and 65-71 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) ☐ Claim(s) _____ is/are allowed.
 6) ☒ Claim(s) 48-63 and 65-71 is/are rejected.
 7) ☐ Claim(s) _____ is/are objected to.
 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date _____.
 4) ☐ Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____.
 5) ☐ Notice of Informal Patent Application (PTO-152)
 6) ☐ Other: _____.

Application/Control Number: 09/825,989
Art Unit: 1614

Page 2

Detailed Action

The following is responsive to applicant's amendment received April 19, 2005.

Claims 1-47 and 64 are cancelled. Claims 48-63, 65-71 are currently pending.

The previous claim rejection under 35 USC 112, second paragraph, set forth in paragraph 1 of the office action mailed Jan. 27, 2005 is withdrawn in view of applicant's amendment and the remarks contained therein.

However, upon reconsideration of the pending claims with the examiner's supervisor, the following new ground(s) of rejection is respectfully submitted.

The allowability of claims 48-57 are withdrawn in view of the following new ground(s) of rejection based on newly discovered prior art.

New Ground(s) of Rejection

Claim Rejection(s)—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Application/Control Number: 09/825,989
Art Unit: 1614

Page 3

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 48-50, 51-57 rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al., 4,158,656 (already of record) in view of WO 97/07230 ('230).

Jones et al. disclose a method for extracting glucosinolates, the method comprising contacting seed material (rapeseed) with an aqueous-lower alkanol (water-alcohol, i.e. ethanol) solvent solution at a temperature below 600 °C and under conditions so as to prevent enzymatic degradation of the glucosinolates. Jones et al. additionally disclose that the temperature is kept below 600 °C in order to prevent activation of the myrosinase. Please see claim 1; col. 1, lines 3- 6; col. 4, lines 44-63.

Jones et al. do not teach extracting glucosinolates using a mixture of dimethyl sulfoxide, acetonitrile and dimethylformamide. Yet, the examiner turns to WO '230, which discloses a solvent extraction method comprising extracting polyhydroxy-alkanoates from biomass using a mixture of solvents, such as acetonitrile, dimethylformamide and dimethylsulfoxide (please see the abstract; page 6, first ¶ under

Application/Control Number: 09/825,989

Page 4

Art Unit: 1614

Solvent Extraction). The biomass comprises plants, which include agricultural crops such as rapeseed. Please see page 5, Biomass, lines 1-17.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the extraction method of Jones et al. by substituting the aqueous lower-alkanol solvent with the solvent mixture dimethyl sulfoxide, acetonitrile and dimethylformamide as suggested by WO '230 because WO '230 teach that the use of such solvents results in an environmentally friendly and economical process for recovering products from a large-scale biological source (please see page 3, lines 5-7). Such a modification would have been motivated by the reasonable expectation that ???

Concerning claim 49, since successful extraction of glucosinolates is related to the concentration of solvents present, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the prior art extraction method such that the acetonitrile, dimethyl sulfoxide and dimethylformamide are present in an amount to optimize the extraction process.

With respect to claims 50-51, since Jones et al. specify that the temperature of the extraction process remain below 60⁰ C in order to prevent activation of the myrosinase enzyme, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the prior art method such that the extraction process is performed at a temperature which allows for effective isolation of glucosinolates while avoiding unwanted activation of myrosinase enzymes.

Finally, claims 53-57 are taught by WO '230, which discloses treatment of numerous plants from agricultural crops. In addressing the claimed homogenization of

Application/Control Number: 09/825,989

Page 5

Art Unit: 1614

the plant tissue, this is also taught by WO '230, which defines "solvent" as a substance which dissolves another substance to form a uniformly dispersed mixture (solution).

2. Claims 58, 59, 60, 62, 63, 65-67, 68-70, 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al., 4,158,656 in view of Pusateri et al., 5,882,646 and Cho et al., WO 9419948 (all references already of record).

Jones et al. disclose a method for extracting glucosinolates, the method comprising contacting seed material (rapeseed) with an aqueous-lower alkanol (water-alcohol, i.e. ethanol) solvent solution at a temperature below 600⁰ C and under conditions so as to prevent enzymatic degradation of the glucosinolates. Jones et al. additionally disclose that the temperature is kept below 600⁰ C in order to prevent activation of the myrosinase. Please see claim 1; col. 1, lines 3- 6; col. 4, lines 44-63.

Jones et al. do not disclose that the isolated glucosinolates are added to food; however the Examiner refers to (1) Pusateri et al., which disclose that brassica vegetables contain glucosinolates, which are helpful in fighting disease. Pusateri et al. additionally disclose that glucosinolates are converted to isothiocyanates, which are known chemoprotective agents. Please see col. 1, lines 12-24; and (2) Cho et al., which discloses that isothiocyanates such as sulforaphane, isolated from Brassica, are known to detoxify carcinogens. Cho et al. additionally disclose a food product, which contains the sulforaphane. Please see claim 25; the abstract; pages 6-7.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Jones et al. by adding the isolated glucosinolates to food products because, in view of the prior art, especially Cho et al., one of ordinary skill

Application/Control Number: 09/825,989

Page 6

Art Unit: 1614

in the art would reasonably expect that foods supplemented with such chemoprotective agents would serve to reduce the risk of cancer in humans. Furthermore, since the isolation process of Jones inactivates enzymes, such as myrosinase, one of ordinary skill in the art would reasonably expect the glucosinolates to remain intact (i.e. not split into harmful substances). Therefore, such a modification would have been motivated by the reasonable expectation of producing a food product conferred with healthy anticancer properties.

With respect to the claimed food products (claims 68-69), it would have been obvious and well within the capability of the skilled artisan to determine the desired, conventional food products within which to incorporate the glucosinolates. In addressing the claimed homogenization of plant tissue with solvent, homogenization is an art-recognized result-effective variable and it would have been obvious to one of ordinary skill in the art to modify it in the method of the prior art.

Finally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply Jones' extraction method to other sources of plant or seed material with the reasonable expectation that the disclosed method would effectively isolate and extract the desired glucosinolate compounds.

3. Claim 61 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jones in view of Pusateri and Cho as applied to claims 58-60, 62-63, 65-71 above, and further in view of Passey et al., 5,290,578.

Jones, Pusateri and Cho as applied above.

Application/Control Number: 09/825,989

Page 7

Art Unit: 1614

However, these references do not disclose an extraction method using carbon dioxide as the solvent. Yet, the examiner refers to Passey et al., which disclose that supercritical fluid extraction using CO₂ has been previously used to extract oil from oilseeds such as soybeans or rapeseed. Passey et al. additionally disclose that CO₂ is neutral from the point of view of taste, inert and easy to remove after extraction. Please see col. 1, lines 64 to col. 2, line 18.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Jones by substituting the aqueous-lower alkanol solvent solution with CO₂ because one of ordinary skill in the art would reasonably expect CO₂ to effectively extract and isolate glucosinolates from the rapeseed. Furthermore, such a modification would have been motivated by the reasonable expectation of performing an extraction process using a solvent, i.e. CO₂, which is effective, inert and easy to remove after extraction of the glucosinolates.

Conclusion

Claims 48-60, 61, 62-63, 65-71 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybillie Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone

Application/Control Number: 09/825,989

Page 8

Art Unit: 1614

number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM

July 11, 2005


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